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Re: Docket Number 99D-0529; Guidance for Industry on Changes to an Approved NDA or ANDA

On behalf of the Food, Drug, and Cosmetic Packaging Materials Committee of The Society of the Plastics Industry, Inc. (SPI)[1/], we hereby respectfully submit these comments on the above-referenced Guidance for Industry, which was made available in November 1999 (64 *Fed. Reg.* 65716 (November 23, 1999)). The thrust of our comments concerns the heightened reporting requirements applicable to changes within packaging materials for sterile liquid dosage forms.

The Guidance Document reflects those changes outlined in a June 28, 1999 Proposed Rule to amend 21 C.F.R. § 314.70, "Supplements and changes to an approved application." [2/] Currently, Section 314.70 provides for three separate reporting categories for changes to an approved new

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1/ The Society of the Plastics Industry, Inc. is the trade association representing the fourth-largest manufacturing industry in the United States. SPI's 2,000 members represent the entire plastics industry supply chain, including processors, machinery and equipment manufacturers and raw material suppliers. The U.S. plastics industry employs 1.3 million workers and provides $274 billion in annual shipments. Founded in 1937, SPI is the voice of the plastics industry. The Food, Drug, and Cosmetic Packaging Materials Committee is composed of SPI members with special interest and expertise in materials used in packaging for drugs, as well as foods, cosmetics, and medical devices.

2/ The proposal to amend 21 C.F.R. § 314.70 was published in the *Federal Register* in June 1999 (64 Fed. Reg. 34608 (June 28, 1999)).

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drug application: (1) changes that must be reported in a supplemental new drug application (SNDA) and approved before the change is made; (2) changes that must be reported in an SNDA, but which may be made before Agency approval; and (3) changes that do not require Food and Drug Administration (FDA) approval and that may simply be reported in the applicant's annual report. The Proposed Rule would amend Section 314.70 to provide four reporting categories for changes: (1) changes that must be reported in a supplement requiring FDA prior approval ("major changes"); (2) changes that require a supplement submission at least 30 days prior to distribution of the drug product made with the change ("moderate changes"); (3) changes that may be implemented when the Agency receives a supplement (also considered "moderate changes"); and (4) changes that may be described in the next annual report ("minor changes").

The Proposed Rule and the "Guidance for Industry on Changes to an Approved NDA or ANDA" would alter the reporting category applicable to changes within the container/closure system for sterile liquid drugs that are made based on a showing of equivalency to the approved system under a protocol approved in the application or published in an official compendium (for example, the United States Pharmacopeia (USP)). Under paragraph (d)(6) of the current regulation, these changes are described in the annual report and do not require FDA prior approval. Paragraphs (c)(2)(i) and (d)(2)(v) of the Proposed Rule, and the explanation in the Guidance Document would require a supplement to be filed for any change within the container/closure system for a sterile liquid dosage form. This filing requirement would apply even if the change is made based upon a showing of equivalency to the approved system under a protocol approved in the application or published in an official compendium.

The Agency has not provided any rationale for its proposal to require a supplement to be filed in connection with any change within a packaging material for a sterile liquid drug, even in situations in which the change is based on a showing of equivalency to the approved system under a protocol approved in the application or published in an official compendium. This requirement, in effect, would mandate duplicative FDA review of equivalency protocols in some cases, and would undermine the utility of USP monographs in others.

In cases in which an equivalency protocol is provided in a new drug application, that protocol is reviewed by the Agency in connection with the application. The Agency has the ability to review the protocol at that time to determine whether it is sufficient to demonstrate equivalency for packaging the types of drugs covered by the application, including sterile liquid dosage forms if they are the subject of the application. Once the application is approved, the applicant considers that an equivalency protocol in the application has been shown, to FDA's satisfaction, to demonstrate the equivalency of a packaging material. It is unduly burdensome to subject a change made based on that protocol to an additional FDA review and approval prior to implementation.

In the same way, it is unnecessary to require FDA prior approval of a change within a container/closure system for a material based on a determination of equivalency made in accordance with a USP monograph that is specifically designed for that purpose. For example, the USP monograph for "Polyethylene Terephthalate Bottles and Polyethylene Terephthalate G Bottles" provides standards and tests to characterize PET and PETG bottles "that are interchangeably

suitable for packaging liquid oral dosage forms." (*See* United States Pharmacopeia 24 Part <661> p. 1934 (2000 ed.).) FDA is provided with the opportunity to review and comment on USP monographs before they are published in final form; thus, the requirement for an additional Agency prior review of a change made in accordance with a USP monograph is redundant.

Consequently, we respectfully request that FDA amend the language of Section IX of the Guidance Document to continue allowing companies to make changes within packaging materials for all types of drugs, including sterile liquid drugs, based on a showing of equivalency to the approved system under a protocol approved in the application or published in an official compendium. Further, we reiterate here our comment to the Proposed Rule to amend 21 C.F.R. § 314.70[3/] that FDA amend the language of paragraphs (c)(2)(i) and (d)(2)(v) of the Proposed Rule to continue to permit companies to make changes within packaging materials for all types of drugs, including sterile liquid drugs, based on a showing of equivalency to the approved system under a protocol approved in the application or published in an official compendium.

SPI appreciates the opportunity to comment on FDA's Guidance for Industry on Changes to an Approved NDA or ANDA. The Society would be pleased to respond to requests from the Agency for additional information pertaining to these comments.

Respectfully submitted,

THE SOCIETY OF THE PLASTICS
INDUSTRY, INC.

By: _____
Ralph A. Simmons

[3/] Comments to the Proposed Rule were submitted to Docket Number 99N-0193 on September 14, 1999 on behalf of SPI.

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